REMARKS

Applicants acknowledge with appreciation the time and courtesies extended by the examiners toward Applicants' representatives during a telephone interview conducted with Applicants' representative on Thursday, December 9, 2004. The examiners' insights and comments have advanced the prosecution of the case. In particular, the outstanding 35 U.S.C. §112, first paragraph and 35 U.S.C. §103(a) rejections were discussed and ways that Applicant's representative can achieve further clarity in responding to the examiners' outstanding rejections.

Applicants address the examiner's remarks in the order presented in the Office Action (dated August 13, 2004). All claim amendments are made without prejudice and do not represent an acquiescence in any ground of rejection.

STATUS OF THE CLAIMS

Claims 1-42 are pending in the application. Claims 1, 3-5, 8, 13, 16, 18-25, 28-32, and 39 have been amended. Claims 6, 7, 9-12, 14-15, 33-38, and 42 have been cancelled. With this amendment, claims 1-5, 8, 13, 16-32, and 39-41 will be pending and claims 6, 7, 9-12, 14-15, 33-38, and 42 are canceled without prejudice to pursuing the claims in a continuing application. Support for the amendments to claims can be found in the claims as originally filed and throughout the application as filed. For example, additional support for "a retrovirus, wherein the retrovirus is the Human Immunodeficiency Virus" and generally "Human Immunodeficiency Virus" can be found at page 19, lines 1-15. Support for "base substitution, and an epigenetic mutation" can be found at page 20, lines 1-6. No new matter is added by the amendments.

Applicants note that the examiner agreed with Applicants' argument filed on June 14, 2004 that at least Group I and II should be rejoined into one group. The examiner, therefore rejoined claims 28-32 for prosecution on the merits.

Claims 1-6, 8-10, 14-32, and 39-42 are rejected under 35 U.S.C. §112, first paragraph, as lacking enablement. Claims 1-13, 16-18, 23-28, and 39-42 are rejected under 35 U.S.C. §103(a) as being unpatentable over Harrigan *et al.*, 1999, *AIDS* 13: 1863-1871) in view of Ioannidis *et al.*, 1998, *American Journal of Epidemiology* 147: 464-471.

REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1-6, 8-10, 14-32, and 39-42 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. More specifically, the examiner stated that the specification, while being enabling for a method of determining a phenotype of a biological sample containing HIV, does not reasonably provide enablement for a method of determining any known phenotype from a mutation pattern phenotype. The examiner also holds the view that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the pending claims.

The enablement requirement of 35 U.S.C. § 112 mandates that the specification teach those skilled in the art how to make and use the claimed invention without undue experimentation. *See In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). The test of enablement is **not** simply whether experimentation would have been necessary, but whether such experimentation would have been **undue**. *See In re Angstadt*, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *See Wands*, 8 U.S.P.Q.2d at 1404.

Applicants respectfully note that the Examiner bears the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide reasonable expectation as to why scope of protection provided by claim is not adequately enabled by disclosure); MPEP § 2164.04. The MPEP further states that a specification **must** be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. *Id.* at 224. The MPEP also quotes *In re Marzocchi*, which states in relevant part:

> [I]t is incumbent on the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

439 F.2d at 224, 169 USPQ at 370.

Applicants believe that the present rejection does not meet the *Marzocchi* standard, as articulated in the MPEP.

However, in order to expedite prosecution of this application, Applicants have amended claims 1, 3-5, 8, 12-13, 16, 18-25, 28-32, and 39 for further clarity and consistency of claim language. Furthermore, Applicants canceled claims 6, 9, 10, 14 and 42 to move the prosecution forward.

Without acceding to the propriety of the rejection of the pending claims under 35 U.S.C. § 112, first paragraph, Applicants respectfully request reconsideration of claims 1, 3-5, 8, 12-13, 16, 18-25, 28-32, and 39 as amended. For these reasons, Applicants request the examiner to withdraw the rejection of pending claims 1-6, 8-10, 14-32, and 39-42 under 35 U.S.C. § 112, first paragraph.

REJECTIONS UNDER 35 U.S.C. §103(A)

Claims 1-13, 16-18, 23-28, and 39-42 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Harrigan *et al.*, 1999, *AIDS* 13: 1863-1871) in view of Ioannidis *et al.*, 1998, *American Journal of Epidemiology* 147: 464-471. Applicants traverse.

The examiner stated that Harrigan *et al.* teach a baseline HIV drug resistance profile for predicting response to ritonavir and saquinavir protease inhibitor therapy.

More specifically, with regards to claims 1 and 28, the examiner is of the opinion that Harrigan *et al.* teach that resistance to 10 different antiviral agents was assessed by both phenotype and genotype. The resistance inferred from the viral genotype was similar to measured phenotypic resistance for both ritonavir and saquinavir (page 1, paragraph 1 and 2). The collection of genotypic and phenotypic data allows correlation to be made with each other. Data were obtained from baseline genotypes using virtual phenotype, assignments of resistance, non-resistant/sensitive or resistant-possible of the Vircogen software (see Tables 3 and 4).

Regarding claims 2 and 40, the examiner states that resistance was measured for 10 different antiviral agents.

Regarding claim 3, the examiner states that resistance was measured to ritonavir and to saquinavir (page 1, paragraph 2).

Regarding claim 4, the examiner stated that Harrigan *et al.* teach plasma samples were used (page 1863, paragraph 2).

Regarding claims 5-7 and 9-12, the examiner holds the view that HIV drug resistance was measured.

Regarding claims 8, 13,16, and 18, the examiner believes the protease codons were assessed for multiple mutations (page 5).

Regarding claims 23 and 24, the examiner states that the amount of drug required to inhibit viral production by 50% (IC50) was determined by an MIT dye reduction assay in MT-4 cells. The IC_{50} is compared to control laboratory, wild-type, virus. An increase greater that four-fold was defined as resistant.

Regarding claims 25-27 and 41-42, the examiner holds the view that Harrigan *et al.* teach that the HIV method for drug resistance creates a profile for clinical use.

The examiner admits that Harrigan *et al.* do not specifically teach searching a relational database. However, the examiner references Ioannidis *et al.* as teaching the use of neural networks to model complex immunogenetic associations of disease. In particular, the examiner points out that HLA data on class I and II alleles and TAP variants from two cohort studies of HIV seroconverters were used to train a neural network for use in establishing the progression of HIV in the set or patients.

Therefore, according to the examiner, it would have been *prima facie* obvious to one of skill in the art at the time of the invention to employ the neural network of Ioannidis *et al.* for the assessment of predicting drug resistance of HIV, as is done by Harrigan *et al.* The motivation to use a neural network is allegedly provided in the statement by Ioannidis *et al.*, which recites, "neural networks could be trained to recognize genetic patterns in conjunction with associated clinical outcomes, and their performance in modeling these complex associations in a training set was superior to logistic regression models." (page 469, column 1). The examiner points out that Harrigan *et al.* use logistic regression in their assessment of baseline resistance; however, the examiner is of the opinion that it would have been obvious to improve the accuracy of the resistance testing by using the neural network of Ioannidis *et al.* for the reasons discussed above. Applicants traverse for the following reasons.

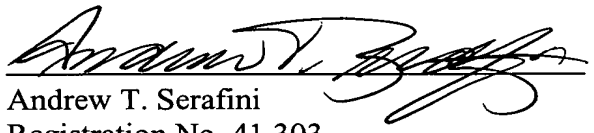
The examiner's combination of the method of Harrigan *et al.* (as noted above the examiner admits that Harrigan *et al.* do not specifically teach searching a relational database;

more specifically, Harrigan *et al.* is silent with respect to searching a genotype/phenotype database for at least one database mutation pattern and predicting the associated phenotypic resistance) with the method of Ionnadis *et al.* (neural networks) clearly has nothing to do with the present invention. The present invention involves a relational database but not the use of any artificial intelligence tool such as neural networks or fuzzy logic. Reconsideration is respectfully requested. Accordingly, Applicants respectfully request that the rejection of claims 1-13, 16-18, 23-28, and 39-42 under 35 U.S.C. § 103 be withdrawn.

The foregoing represents a *bona fide* attempt to advance the present case to allowance. Applicant submits that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are respectfully requested. If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-332-1380.

Respectfully submitted,

Date: December 13, 2004



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